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10/581,274	05/30/2008	**David John Grainger**	P71304US0	1913

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JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER	
VAKILI, ZOHREH	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,274	GRAINGER ET AL.	
	Examiner	Art Unit	
	ZOHREH VAKILI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/03/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-26 are presented for examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-2, 7-14, 19, and 21-23 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. This claim is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). The term "use of" is not among the statutory class of inventions. These claims are rejected as "use" claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 7-14, 19, and 21-23 provide for the use of a compound, but, since the claim does not set forth any steps involved in the compound/process, it is unclear what compound/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compound of formula I, wherein compounds claimed in claims 15, 16, 17, 18, 21, 22, 23, 24, 25, and 26 are synthesized from the general formula I does not reasonably provide enablement for making the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connect, to make the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

7) the state of the prior art; and,

8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The presently claimed invention is directed to a compounds of formula I

The instant claims requires synthesizing compound formula I to produce the compounds I'. However, the instant specification as originally filed lacks adequate guidance, direction or discussion to apprise the skilled artisan of the specific conditions and/or starting materials and/or reaction schema to be used to synthesize the claimed compounds of the general formula and compounds of formula I'. In the absence of such direction or guidance, the instant specification fails to provide adequate enabling disclosure to practice the full scope of the claimed subject matter.

The disclosure has been fully and carefully considered, it is noted that this same disclosure lacks a clear teaching, direction or guidance as to how to prepare compounds of the instantly claimed general formula. There are none specific teaching to the synthesis of the particular compound under examination and none specific schema in the instant disclosure to provide a method of

synthesizing a compound of the structure presently under examination. Moreover, even if this information were actually contained within organic chemistry texts, this information regarding the manner and process of synthesizing the claimed compound is essential subject matter for the practice of the instant invention and cannot be properly incorporated into the instant specification be reference to, e.g., a publication, for such essential subject matter.

Applicant is reminded that the incorporation of essential material in the specification by reference to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. Please see 37 C.F.R. 1.57(f).

Furthermore, it is noted that the execution of chemical reactions is dependent upon numerous variable factors that are essential for producing the intended compound, such as, but not limited to, the starting materials to be employed, the temperature at which the reaction(s) should be carried out, solvents, reaction catalysts, molar quantities, surface area, pressure, activation energies, etc. In view of such a number of factors, and further in view of the high degree of variability for each single factor that must be taken into account in

order to provide an accurate means for producing the claimed compounds of the general formula, the state of the art with regard to chemical reactions in general is highly complex and sufficiently unpredictable such that the skilled artisan would have been required to undertake undue experimentation to determine the exact conditions and manner and/or process of execution to arrive at those conditions that would have been amenable to actually producing the compound of the general formula and detailed guidance to this effect.

Absent such evidence or reasoning, and further absent any direction or guidance as to how the skilled artisan would go about synthesizing the claimed compound of the general formula, one of ordinary skill in the art would have no alternative recourse but to undertake an exhaustive, and, thus, unduly burdensome, search for ways to synthesize this embodiment of the claimed invention suitable for use in practicing the claimed process, particularly since the skilled artisan is faced with such a breadth and variety of possible starting materials and reaction schema from which to choose. In addition, it is not readily apparent that the prior art recognized methods of synthesizing the presently claimed compound at the time of the invention (or at least Applicant has failed to point to such information in a document that can be properly incorporated by reference) such that one of ordinary skill in the art would have been able to drawn upon the knowledge already present in the prior art to execute the synthesis of the presently claimed compound of the general formula, absent factual evidence to the contrary.

Applicant has (1) failed to provide any clear general synthetic procedures

to the instantly claimed compound of the general formula or (2) failed to provide any working or prophetic examples directed to a possible method and/or manner of synthesis for the instantly claimed compound of the general formula. While the lack of a working embodiment cannot be the *sole* factor in determining enablement, the absence of substantial evidence commensurate in scope with the breadth of the presently claimed subject matter, in light of the unpredictable nature of the art and the limited direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the prior art and Applicant's disclosure and remarks that experimentation in this particular art is not at all uncommon, but that the experimentation required in order to practice this aspect of the invention would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*." (emphasis added)

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of scientist with several years of experience in the art.

As the discussion of the above factors establish, practicing the claimed invnetion in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation or ability to make the full scope of the

invention as instantly claimed, given the disclosure and supporting examples provided in the present specification and the state of the art at the time of the invention. In order to actually achieve the claimed invention, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the embodiments presently claimed.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the prophylaxis of the symptoms of an inflammatory disease. The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) As to undue experimentation.

The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1) the nature of the invention; the invention is directed to a composition and method for the prophylaxis of the symptoms of an inflammatory disease.

2) the breadth of the claims; the scope of the composition and method for the prophylaxis of the symptoms of an inflammatory disease.

3) the predictability or unpredictability of the art; the art does not enable a person of ordinary skill in the art to make and use the claimed invention without resorting to undue experimentation. The burden of enabling one skilled in the art for the prophylaxis of the symptoms of an inflammatory disease is much greater than that enabling the treatment. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of the prophylaxis of the symptoms of an inflammatory disease.

. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for method for the prophylaxis of the symptoms of an inflammatory disease. No experimental evidence or mechanism of action for supporting a method for the

prophylaxis of the symptoms of an inflammatory disease. using the specified actives would actually provide a method for the prophylaxis of the symptoms of an inflammatory disease by simply administering, by any method, an amount of the claim specified active agents. The specification fails to enable one of ordinary skill in the art to practice the presently claimed composition for a method for the prophylaxis of the symptoms of an inflammatory disease.

The term "prophylaxis" circumscribes methods of treatment having unpredictability and undue experimentation. Since prophylaxis is not as of yet reasonably possible with most diseases/disorders. The specification is viewed as lacking an adequate enablement of where the method of prophylaxis of the symptoms of an inflammatory disease.

4) the amount of direction or guidance presented; the specification and the example does not provide any guidance in terms for the method of prophylaxis of the symptoms of an inflammatory disease.

5) the presence or absence of working examples; no working examples are provided for the method of prophylaxis of the symptoms of an inflammatory disease, for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the prophylaxis effects of the instant composition and method. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

6) the quantity of experimentation necessary; the quantity of experimentation would be an undue burden to one of ordinary skill in the art and amount to the trial and error type of experimentation. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant composition and method claims. In view of the breadth of the claims, the chemical nature of the invention and unpredictability for the method of prophylaxis of the symptoms of an inflammatory disease, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-6, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an Enablement rejection.

The specification does not reasonably provide enablement for making and using the pharmaceutical composition comprising the active compound of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v.

Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1) the nature of the invention; state of the prior art; relative skill of those in the art; and the predictability of the art;

The invention is directed to a pharmaceutical composition and method for treating inflammatory diseases. The claimed invention does not relate to treating a subject. Various diseases having various different causes are not treatable by a single composition. Given the great diversity between various diseases (viral infections, bacterial infection, cancers, autoimmune diseases, clogged arteries, neurological diseases, etc.), the unpredictability of treating an

animal (e.g., no specific disease) has a number of facets, as discussed hereinafter.

A. Treatment of Disease Type

While the state of the art is relatively high with regard to the treatment of specific diseases with a specific agent, it is long underdeveloped with regard to the treatment of an animal broadly, that is, general treatment, with no specific disease combined with a specific drug therefore. In particular, there is no known "treatment" drug, that can treat, "all that ails you". This is why the National Cancer Institute (NCI) has the extensive *in vitro* drug-screening program it does. As discussed by the court in In re Brana, 51 F.3d 1560 (Fed. Cir. 1995), *in vitro* assays are used by NCI (such as the P388 and L1210 lymphocytic leukemia tests at issue therein) to measure the potential antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) *Id.* at 1567-68. These *in vitro* tests are considered reasonably correlative of success *in vivo*.

Thus, a considerable amount of *in vitro* empirical testing is required, with no *a priori* expectation of success being present, before a candidate for even treating a specific disease, such as, breast cancer.

B. The therapeutic agent used

The therapeutic agent has no correlation treating which diseases. Thus, it is

unclear, which type of inflammatory disease this drug is going to treat.

2) the breadth of the claims; the scope of the composition claim does not include what specific disease its active compound is to treat. The claims are very broad it only indicates inflammatory disorder.

3) the predictability or unpredictability of the art; the art does not enable a person of ordinary skill in the art to make and use the claimed invention without resorting to undue experimentation. The burden of enabling one skilled in the art to a pharmaceutical composition comprising the active compound would be much greater than that enabling the treatment. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of treating other inflammatory diseases. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for treating other types of inflammatory diseases. No experimental evidence or mechanism of action for supporting treating all types of inflammatory diseases using the specified actives by simply administering, by any method, an amount of the claim specified active agents. The specification fails to enable one of ordinary skill in the art to practice the presently claimed composition for treating the risk of all types of inflammatory diseases. It is unpredictable to practice with a mammalian subject treating for all types of inflammatory diseases with a chemical administration as instantly claimed. The specification is viewed as lacking an adequate enablement of where all types of inflammatory diseases may be actually treated.

4) the relative skill of those in the art; the relative skill of those in the art of

pharmaceuticals is high.

5) the amount of direction or guidance presented; the specification and the example does not provide any guidance in terms of treating other types of inflammatory diseases.

6) the presence or absence of working examples; no working examples are provided for treating all types of inflammatory diseases with the same compound, for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

7) the quantity of experimentation necessary; the quantity of experimentation would be an undue burden to one of ordinary skill in the art and amount to the trial and error type of experimentation. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant process claims. In view of the breadth of the claims, the chemical nature of the invention and unpredictability of treating all types of inflammatory diseases in a mammal, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims. The lack of adequate guidance from the specification or prior art with regard to the actual

treatment fails to rebut the presumption of unpredictability present in this art. Applicants fail to provide the guidance and information required to ascertain which particular disease the claimed agent will be effective against without resorting to undue experimentation. Applicant's limited disclosure of the treatment of is not sufficient to justify claiming all treatment broadly.

In consideration of each of factors 1-7, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 102

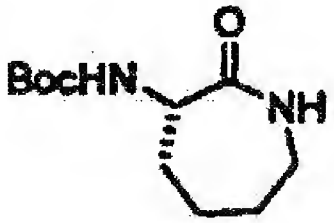
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Seiffert et al. (Presenilin-1 and -2 are Molecular targets for gamma-Secretase Inhibitors, The Journal of Biological Chemistry, Vol. 275, No. 44, 2000, pages

34086-3409) (cited n IDS).

Seiffert et al. discloses the compound of the instant claimed invention for the treatment of Alzheimer's disease (see abstract and page 34087).



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Consequently, the reference anticipates the claimed invention defined in claims 1-26

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zohreh Vakili whose telephone number is 571-272-3099. The examiner can normally be reached on 8:30-5:00 Mon.-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Zohreh Vakili

Patent Examiner June 15, 2010
1614

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614